Early Journal Content on JSTOR, Free to Anyone in the World

This article is one of nearly 500,000 scholarly works digitized and made freely available to everyone in the world by JSTOR.

Known as the Early Journal Content, this set of works include research articles, news, letters, and other writings published in more than 200 of the oldest leading academic journals. The works date from the mid-seventeenth to the early twentieth centuries.

We encourage people to read and share the Early Journal Content openly and to tell others that this resource exists. People may post this content online or redistribute in any way for non-commercial purposes.

Read more about Early Journal Content at http://about.jstor.org/participate-jstor/individuals/early-journal-content.

JSTOR is a digital library of academic journals, books, and primary source objects. JSTOR helps people discover, use, and build upon a wide range of content through a powerful research and teaching platform, and preserves this content for future generations. JSTOR is part of ITHAKA, a not-for-profit organization that also includes Ithaka S+R and Portico. For more information about JSTOR, please contact support@jstor.org.

THE PRODUCTION OF ANTIRABIC IMMUNITY BY INTRA-SPINAL INJECTIONS OF VIRUS.*†

D. L. HARRIS.

(From the Municipal Laboratory of Pathology and Bacteriology, Hospital Department, City of St. Louis.)

The object of this paper is to present the results of an attempt to produce a rapid antirabic immunity by direct immunization of the brain cells.

The method devised by Pasteur for the prevention of hydrophobia limited this work to large and well equipped laboratories, and required that the patient undergo treatment for a period of three weeks or more. Several modifications have been adopted from time to time which have made the work of preparing the material less onerous, and the treatment more available to the public, especially to those patients living at a distance from such a laboratory. In all antirabic institutes, whatever modification may have been adopted in the preparation of the material, the treatment consists in a number of injections into the abdominal wall. The result of this is an indirect immunization of the brain cells against the infective agent. In spite of all treatment, however, a small number of the patients die before immunity can be established.

During the past year I have described a method[1] for preserving the virus used in antirabic immunization. This, in brief, consists in freezing with carbon dioxid snow the brain and cord of a rabbit infected with the disease, and drying these in a vacuum at a temperature of — 10° C. Material prepared in this manner and kept free from moisture in an ice box (10° C.) loses its infectivity so slowly that after a preservation of 40 weeks one-tenth of a milligram when injected subdurally will produce paresis in a rabbit in seven days. In other words, after eight months of desiccation its infectivity is equal to that of Pasteur's two-day cord.

---

* Received for publication October 4, 1912.

† Read before the International Congress on Hygiene and Demography, Washington, D.C., September 24, 1912.

[1] *Jour. Infect. Dis.*, 1912, 10, p. 369.

In testing the desiccated material from time to time to determine the effect of time, temperature, and light on the rate of loss of infectivity, I observed that some rabbits which had received subdurally a quantity of the virus slightly less than the minimal infective dose developed an appreciable and determinable immunity against subsequent subdural inoculations.

Ten rabbits were immunized in this manner and the degree of immunity thus acquired was ascertained by one or more later tests. Of these ten, six resisted an injection sufficient to kill untreated controls. One did not develop the disease after an injection of twice the minimal infective dose. One survived the injection of 100 M.I.D. Two died on the 15th and 17th days, respectively, after the injection of twice the minimal infective dose.

Of seven rabbits that survived the first test, four were inoculated later with 10 M.I.D. of street virus. Two survived and two died on the 18th day. All injections were made under the dura after trephining. Table 1 gives the results of these experiments in detail.

TABLE 1.

Rabbit	Amount of First Inoculation	Time of Second Inoculation	Amount	Time of Third Inoculation	Amount	Result
1.............	½M.I.D.	30 days	2 M.I.D.	....	....	Died 15th day
2.............	¼ "	58 "	2 "	....	....	" 17th "
3.............	⅔ "	29 "	2 "	....	....	Immune
4.............	½ "	43 "	1 "	72 days	10 M.I.D. s.v.	Died
5.............	½ "	43 "	1 "	72 "	10 " "	"
6.............	⅓ "	27 "	1 "	78 "	10 " "	Immune
7.............	¼ "	27 "	1 "	107 "	10 " "	"
8.............	½ "	78 "	1 "	107 "	100 " "	Died
9.............	⅒ mg.	27 "	1 "	107 "	200 " "	"
10.............	¼ "	36 "	100 "	55 "	200 " "	"

Tests made in one lot of material which had been kept for some months at room temperature in daylight showed this to be non-infective, and it was observed that the rabbit inoculated with this material had also acquired an immunity (Table 1, rabbit No. 9).

Following this, a number of rabbits were given larger quantities of non-infective material intraspinally.

In these experiments, the details of which will be seen in Table 2, rabbits Nos. 1, 2, and 3 were injected intraspinally with material which had been kept in an ice box for 66 days and then in the light at room temperature for 219 days. Rabbits Nos. 4, 5, and 6 were injected with material that had been kept in a north window, room temperature, for eleven months. When these six were injected the technic of making the spinal puncture was undeveloped and it was suspected at the time that the needle had not entered the spinal canal of rabbits Nos. 1 and 4. Their susceptibility to a later inoculation of 4 M.I.D. showed this suspicion to have been well founded. Rabbits Nos. 7 to 19 were injected with material which had been in the dark at room temperature for eight months. Rabbits Nos. 20 to 23 were injected with material which had been kept in the presence of P_2O_5, which, it has been demonstrated, causes a relatively rapid destruction of virulence.

TABLE 2.

Rabbit	Amount Injected	Time of Inoculation	Amount	Result
1	20 mg. f.v.	10 days later	4 M.I.D. f.v.	Died
2	20 “ “	10 “ “	4 “ “	Immune
3	20 “ “	10 “ “	4 “ “	“
4	20 “ “	10 “ “	4 “ “	Died
5	20 “ “	10 “ “	4 “ “	Immune
6	20 “ “	10 “ “	4 “ “	“
7	25 “ “	same time	1 “ “	“
8	20 “ “	“ “	2 “ “	“
9	5 “ “	4 days later	5 “ “	“
10	20 “ “	4 “ “	10 “ “	Died
11	5 “ “	6 “ “	10 “ “	“
12	10 “ “	6 “ “	15 “ “	Immune
13	15 “ “	6 “ “	10 “ “	“
14	5 “ “	8 “ “	20 “ “	Died
15	10 “ “	8 “ “	20 “ “	“
16	10 “ “	8 “ “	30 “ “	“
17	15 “ “	8 “ “	20 “ “	Immune
18	20 “ “	14 “ “	20 “ “	Died
19	20 “ “	15 “ “	10 “ “	Immune
20	20 “ “	same time	2 “ “	Died
21	20 “ P_2O_5	14 days later	5 “ “	Immune
22	20 “ “	14 “ “	10 “ “	Died
23	20 “ “	14 “ “	20 “ “	“
24	12 “ s.v.	same time	4 “ “	“
25	12 “ “	14 days later	10 “ “	“
26	20 “ “	14 “ “	20 “ “	“
27	12 “ “	28 “ “	10 “ “	Immune
28	20 “ f.v.	11 “ “	10 “ “	“
29	25 “ “	44 “ “	10 “ “	“

Rabbits Nos. 24 to 27 were injected with desiccated street virus whose infectivity had been destroyed by placing it in direct sunlight (west window) for three weeks. The virus was obtained from a case of rabies in a woman and the material was the brain of a rabbit, first passage. It had been desiccated five months. It will be seen that three of these rabbits were not immune to 10 M.I.D. 14 days after the injection, but that the fourth resisted a similar inoculation 28 days later. The action of direct sunlight may have been a factor in lessening the immunizing capacity of the material. It is of interest to note that street virus may be used for immunization by this method.

Rabbit No. 28 was injected subdurally (trephine) with material which had been kept in an ice box for seven months and in one of the laboratory rooms in daylight for 39 days. Rabbit No. 29 is the same as No. 7 and after surviving this test was reinoculated 44 days later.

These experiments show that the brain of a rabbit may be directly immunized by a single intraspinal injection of non-infective material to such a degree that two weeks later the animal successfully withstands a subdural injection of 10 to 20 times an otherwise fatal dose. The immunity is acquired so rapidly that the intraspinal injection of five milligrams or more will protect against a simultaneous inoculation of a minimal infective dose injected subdurally (trephine).

Similar experiments were made on dogs as follows: Three dogs were injected by lumbar puncture with 50 mg. of non-infective material and 16 days later were inoculated under the dura with 1–10 mg. of the medulla of a rabid dog (desiccated).

In another series, one dog was given 10 mg. of a non-infective desiccated brain; two dogs 20 mg.; two dogs 40 mg.; and five were inoculated eight days later with 1–10 mg. of desiccated street virus. Two other dogs were injected with 50 mg. and 25 mg. intraspinally and at the same time were inoculated under the dura with 1–10 mg. of desiccated street virus. Two dogs were used as controls. The estimated amount of infective virus received by each of these twelve dogs was five times the infective dose for rabbits.

One of the control dogs developed furious rabies on the fourteenth day. The other control became emaciated five weeks later, refused food on the 44th day, and died on the 46th day after a paralysis which developed a few hours earlier. The autopsy did not reveal any cause of death and Negri bodies were not found in the brain. One of the two dogs inoculated and immunized at the same time became extremely emaciated five weeks later, developed paralysis on the 36th day, and died on the 38th day. The remainder of the immunized dogs have shown no recognizable injury following the inoculation.

The above experiments seem to show that it is comparatively easy to immunize rabbits against rabies by a single intraspinal injection of non-infective desiccated "virus," and that the resulting immunity is acquired with surprising rapidity. The test on the dogs is somewhat unsatisfactory because the amount inoculated was too small to produce a definite and early outbreak of the disease in both control animals. It does appear, however, that the intraspinal injection is not followed by any ill results.

Whether or not fixed virus may be rendered non-infective by methods other than one I have employed without, at the same time, lessening its immunizing value, is a question which offers an opportunity for further investigation. It appears that the material whose infectivity was destroyed by P_2O_5 and by direct sunlight did not have so great an immunizing value as the material which had been allowed to die more slowly.

If further investigations show that the intraspinal injections of this material are harmless to. animals, and that immunity is regularly and rapidly conferred, we may be in possession of a means of saving some of those patients who have received severe injuries about the face, and who now succumb in spite of the treatment employed at the present time. Another advantage of this method is that the immunizing property of the material I have used is not affected by age, and it may be stored in quantities and kept anywhere for immediate use.